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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,102	07/17/2000	NICHOLAS THOMAS	PA9720	9263

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PATENT DEPARTMENT
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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 11/12/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,102	THOMAS, NICHOLAS	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-9 and 12-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-9 and 12-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 7/25/03 in Paper No. 14 is acknowledged and has been entered. Claim 11 has been cancelled. Claims 1 and 6 have been amended. Claims 12-18 have been added. Accordingly, claims 1, 3, 5-9, and 12-18 are pending and are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 112/102/103

2. The rejections of claim 11 are now moot in light of Applicant's cancellation of the claim.

Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 3, 5-9, and 12-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step d) is vague and indefinite in reciting, "such that a portion of said signal moiety is caused to be bound to said first component" because it is unclear what

"portion" of said second component is caused to be bound to the first component. Does Applicant intend the claimed "portion" to be the second component carrying the signal moiety, since it is the second component that is a member of the binding pair; thus, causing the signal moiety to be bound to the first component.

Claim 1, step f), parts i) and ii), remain vague and indefinite because it is unclear how the signal moiety and the detectable label are measured and determined differentially, so as to provide a measure of the presence or absence of the compound being tested, concentration of the compound being tested, and biological activity of the compound to being tested, as well as an indication of each of the samples containing the compound being tested. Specifically, step a) recites that the reactant bound to the carrier beads are the same, and in step d) the same reagents are provided in all of said N different reaction vessels. Accordingly, it is unclear how cross-reactivity is prevented between the N samples, the (same) reactants bound to the beads, and the added (same) reagents, upon combining the contents of the N different reaction vessels into a mixture, especially in the presence of unbound components left from the binding assay. Further, whilst each sample is said to contain a single compound in the preamble, it is unclear where in the claim the compound is recited to take part in the binding assay so as to effect measurement of its presence or absence or concentration. Lastly, it is unclear how biological activity is measured differentially since biological activity requires intracellular function measurement.

Claim 6 lacks antecedent basis in reciting, "the ... reagent".

Claim 12, step f), parts i) and ii), remain vague and indefinite because it is unclear how the signal moiety and the detectable label are measured and determined differentially, so as to provide a measure of the presence or absence of the compound being tested, concentration of the compound being tested, and biological activity of the compound to being tested, as well as an indication of each of the samples containing the compound being tested. Specifically, step a) recites that the reagent bound to the carrier beads are the same, and in step d) the same additional reagents are provided in all of said N different reaction vessels. Accordingly, it is unclear how cross-reactivity is prevented between the N samples, the (same) reactants bound to the beads, and the added (same) reagents, upon combining the contents of the N different reaction vessels into a mixture, especially in the presence of unreacted components left from the assay. Further, whilst each sample is said to contain a single compound in the preamble, it is unclear where in the claim the compound is recited to take part in the assay so as to effect measurement of its presence or absence or concentration. Lastly, it is unclear how biological activity is measured differentially since biological activity requires intracellular function measurement.

Claim 15 lacks antecedent basis in reciting, "the ... reactant".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1, 3, 5-7, 9, 12-16, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chandler et al. (US 5,981,180) in view of Yamashita et al. (US 6,210,900).

Chandler et al. disclose multiplexed analysis of samples each containing test compounds (analytes) (see column 7, lines 25-61). Chandler et al. disclose providing populations of carrier beads (beadsets or bead subsets) labeled with an appropriate reactant such as a biomolecule or a DNA sequence (see column 7, line 63 to column 6, line 9). Each population of beads is homogeneous and differing in at least one distinguishable parameter from other populations. Distinguishable parameters include size, shape, labels which have fluorescent emissions in more than one wavelength resulting from the presence of two or fluorochromes on the beads, etc. The classification parameter for each population is known and therefore the identity of each population can be verified using flow cytometry (see column 3, line 65 to column 4). Each bead population is coated with different reactants so as to bind or react and detect different compounds. For more quantitative analysis of compounds and biological activity (kinetic studies), each population of beads may be coated with a same reactant but at different concentrations so as to produce populations varying in density of precoated reactant rather than type of reactant; thereby allowing a parameter to serve as an indicator of reactant identity or reactant density. Chandler et al. disclose incorporating the beads and reagents into a kit format.

Chandler et al. differ from the instant invention in failing to disclose dispensing one of N populations of carrier beads having reagent bound thereto into N reaction vessels, adding thereto one of N samples into each reaction vessel, then further adding additional reagent for assay reaction; thereafter, the contents of each reaction vessel are combined into a single mixture for analysis using flow cytometry.

Yamashita et al. disclose a method for identifying test compounds having desired characteristics and identifying essential moieties in a lead structure which comprises preparing one or more encoded combinatorial libraries from a specified set of reaction sequences wherein the test compounds are tested for biological activity (pharmaceutical activity). Specifically, Yamashita et al. disclose providing populations of labeled (tagged) beads with fluorescent labeled identifiers attached thereto for encoding the combinatorial libraries (see Summary). Each population of beads is distinguishable from other populations by virtue of size, composition, fluorescent marker, and fluorescent label identifier. The identifier is a "coding" label attached to a population of beads by adding ratios of a fluorophore and a non-fluorophore or adding multiple different fluorophores in varying ratios (see column 3, lines 38-55). Yamashita et al. disclose that the number of readily distinguishable populations of beads correspond to the number of alternative variables in a registry. Yamashita et al. disclose dispensing an entirety of a population in a separate reaction vessel or well of a microtiter plate; beads usually are divided into populations of 1000 or more (see column 4, lines 16-37). Thereafter, appropriate reagents are added to each individual reaction vessel for reaction or assay to take place. After washing, the populations of beads are combined

into a single mixture and subjected to flow cytometry for sorting (see column 4, lines 38-49). The compounds of the library can be tested using samples in a soluble receptor assay (see column 13, lines 1-7).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have combined the reaction samples in the method of Chandler into a single mixture for flow cytometric analysis as taught by Yamashita because Yamashita specifically taught that various encoded or tagged beads that have undergone reaction with a test compound, each individual bead having characteristic parameters, can be combined into a single mixture for flow cytometric analysis which allows for sorting, identification, and analysis based on the their characteristic parameters acquired after exposure with the corresponding compounds from the combinatorial libraries.

5. Claims 8 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chandler et al. (US 5,981,180) in view of Yamashita et al. (US 6,210,900) and in further view of Mandecki (US 5,641,634).

Chandler et al. and Yamashita et al. have been discussed supra. Chandler et al. and Yamashita et al. differ in failing to disclose that the beads populations are electronically labeled.

Mandecki et al. disclose a multiplex assay using electronically encoded carrier beads (solid phase particles associated with transponders) that are assigned a unique index number which can be retrieved by a scanner device at any time during an assay

for a compound. According to Mandecki et al., the carrier beads are analyzed to detect a label indicative of a reaction or binding of the compound to the carrier bead such as fluorescence, color, or radioactivity. Analysis is then preceded or followed by the decoding of the index number from the transponder. Both analysis and decoding can be done using two different instruments : a fluorimeter and a scanner. Mandecki et al. also disclose a kit for detecting biomolecular compounds in samples using carrier beads, assay vessels, coated labeled reagent (see columns 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to further electronically encode the populations of beads as disclosed by Mandecki so as to be an added "another" decipherable parameter in the bead populations in the method as taught by Chandler as modified by Yamashita because Mandecki specifically disclosed its applicability in multiplex assays such as the assay of Chandler. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the transponders of Mandecki into the method of Chandler as modified by Yamashita because Mandecki specifically disclosed their advantage in further detecting and differentiating increased number of analytes simultaneously in comparison to current multiplex assays.

Response to Arguments

6. Applicant's arguments filed 5/25/03 have been fully considered but they are not persuasive.

A) Applicant argues that the samples of Chandler, containing multiple analytes in a single sample, are not the same as Applicant's multiple samples, i.e. "each containing a single compound to be tested".

In response, the recitation "(the samples) each containing a single compound to be tested" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

B) Applicant argues that Yamashita does not teach the use of a method with pre-existing compounds that are not coupled to beads. Consequently, Yamashita does not disclose the dispensing of "samples each containing a single compound to be tested".

In response, claims 1 and 12, as currently recited, do not exclude the teaching of Yamashita since there is no recitation of the application of the compound in the assay, how it structurally relates to the reactant bound to the beads and the reagents added to the N different reaction vessels, and how it is detected therefrom so as to effect measurement. Specifically, the recitation of the compound is limited to the preamble. Additionally, "(the samples) each containing a single compound to be tested" has not

been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

7. For reasons aforementioned, no claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
November 6, 2003

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641